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PRELIMINARY AMENDMENT **Address to:** **Box Patent Application** **Assistant Commissioner of Patents** **Washington, D.C. 20231**	**First Named Inventor**	**David Goldstein**
	Application Number	**(unassigned)**
	Filing Date	**(herewith)**
	Group Art Unit	**(unassigned)**
	Examiner	**(unassigned)**
	Attorney Docket No.	**R0038G-DIV**
	Title	**Pyrazole Derivatives - p38 Map Kinase Inhibitors**

Express Mail Label No. ET 648481815 US

Sir:

Attached herewith is a Preliminary Amendment to the enclosed patent application, which is a divisional application of U.S. Application Serial No. 09/305,737, filed May 5, 1999, which claims the priority benefits of U.S. Provisional Application Serial No. 60/084,250, filed May 5, 1998, U.S. Provisional Application Serial No. 60/122,410, filed March 2, 1999, and U.S. Provisional Application Serial No. 60/130,369, filed April 21, 1999, for "PYRAZOLE DERIVATIVES P38 MAP KINASE INHIBITORS,".

IN THE SPECIFICATION

Please amend the text on page 1, lines 4-6, under the section entitled "CROSS-REFERENCE TO RELATED APPLICATION", as follows:

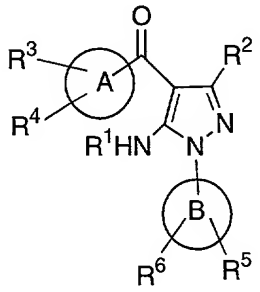
-- This application is a divisional application of U.S. Application Serial No. 09/305,737, filed May 5, 1999 and claims the benefit under 35 U.S.C. 119(e) of U.S. Provisional Application Serial No. 60/084,250, filed May 5, 1998, U.S. Provisional Application Serial No. 60/122,410, filed March 2, 1999, and U.S. Provisional Application Serial No. 60/130,369, filed April 21, 1999, all of which are incorporated herein by reference in their entirety. --

IN THE CLAIMS:

Please amend Claims as follows:

Cancel claims 1, 32 and 36-37.

33. (Amended herein) A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound selected from the group of compounds represented by Formula (I):



(I)

wherein:

R^1 is hydrogen or acyl;

R^2 is hydrogen or alkyl;

A is an aryl ring;

B is an aryl ring;

R^3 is selected from the group consisting of:

(a) amino, alkylamino or dialkylamino;

(b) acylamino;

(c) optionally substituted heterocyclyl;

(d) optionally substituted aryl or heteroaryl;

(e) heteroalkyl;

(f) heteroalkenyl;

(g) heteroalkynyl;

(h) heteroalkoxy;

(i) heteroalkylamino;

(j) optionally substituted heterocyclylalkyl;

(k) optionally substituted heterocyclylalkenyl;

(l) optionally substituted heterocyclylalkynyl;

(m) optionally substituted heterocyclylalkoxy, cycloakoxy or heterocycloxy;

(n) optionally substituted heterocyclylalkylamino;

(o) optionally substituted heterocyclylalkylcarbonyl;

(p) heteroalkylcarbonyl;

(q) $-NHSO_2R^6$ where R^6 is alkyl, heteroalkyl or optionally substituted heterocyclylalkyl;

(r) $-NHSO_2NR^7R^8$ where R^7 and R^8 are, independently of each other, hydrogen, alkyl or heteroalkyl;

(s) -Y-(alkylene)-R^9 where:

Y is a single bond, -O-, -NH- or $-S(O)_n-$ (where n is an integer from 0 to 2); and

R^9 is cyano, optionally substituted heteroaryl, -COOH, $-COR^{10}$, $-COOR^{11}$, $-CONR^{12}R^{13}$, $-SO_2R^{14}$, $-SO_2NR^{15}R^{16}$, $-NHSO_2R^{17}$ or $-NHSO_2NR^{18}R^{19}$, where R^{10} is alkyl or optionally substituted heterocycle, R^{11} is alkyl, and R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18} and R^{19} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(t) $-C(=NR^{20})(NR^{21}R^{22})$ where R^{20}, R^{21} and R^{22} independently represent hydrogen, alkyl or hydroxy, or R^{20} and R^{21} together are $-(CH_2)_n-$ where n is 2 or 3 and R^{22} is hydrogen or alkyl;

(u) $-NHC(X)NR^{23}R^{24}$ where X is -O- or -S-, and R^{23} and R^{24} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(v) $-CONR^{25}R^{26}$ where R^{25} and R^{26} independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclylalkyl, or R^{25} and R^{26} together with the nitrogen to which they are attached form an optionally substituted heterocyclyl ring;

(w) $-S(O)_nR^{27}$ where n is an integer from 0 to 2, and R^{27} is alkyl, heteroalkyl, optionally substituted heterocyclylalkyl, or $-NR^{28}R^{29}$ where R^{28} and R^{29} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(x) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

(y) arylaminoalkylene or heteroarylaminoalkylene;

(z) Z-alkylene-$NR^{30}R^{31}$ or Z-alkylene-OR^{32} where Z is -NH-, -N(lower alkyl)- or -O-, and R^{30}, R^{31} and R^{32} are independently of each other, hydrogen, alkyl or heteroalkyl;

(aa) -OC(O)-alkylene-CO_2H or -OC(O)-NR'R" (where R' and R" are independently hydrogen or alkyl); and

(bb) heteroarylalkenylene or heteroarylalkynylene;

R^4 is selected from the group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl;

(d) alkoxy; and

(e) hydroxy;

R^5 is selected from the group consisting of :

(a) hydrogen;

(b) halo;

(c) alkyl;

(d) haloalkyl;

(e) thioalkyl;

(f) hydroxy;

(g) amino;

(h) alkylamino;

(i) dialkylamino;

(j) heteroalkyl;

(k) optionally substituted heterocycle;

(l) optionally substituted heterocyclylalkyl;

(m) optionally substituted heterocyclylalkoxy;

(n) alkylsulfonyl;

(o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;

(p) heteroalkoxy; and

(q) carboxy;

R^6 is selected from a group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl; and

(d) alkoxy; and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

2. (Amended) The method of Claim 33 wherein R^3 is:

(a) optionally substituted heterocyclyl;

(b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO_2R' (where R' is alkyl) or $SO_2NHR'R''$ (where R' and R" are independently hydrogen or alkyl);

(c) heteroalkyl;

(d) heteroalkenyl;

(e) heteroalkylamino;

(f) heteroalkoxy;

(g) optionally substituted heterocyclylalkyl, or heterocyclyloxy;

(h) optionally substituted heterocyclylalkenyl;

(i) optionally substituted heterocyclylalkynyl;

(j) optionally substituted heterocyclylalkoxy;

(k) optionally substituted heterocyclylalkylamino;

(l) optionally substituted heterocyclylalkylcarbonyl;

(k) -Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -$CONR^{12}R^{13}$, SO_2R^{14}, -$SO_2NR^{15}R^{16}$ -$NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl;

(l) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

(m) arylaminoalkylene or heteroarylaminoalkylene; or

(n) Z-alkylene-$NR^{30}R^{31}$ where Z is -NH-, -N(alkyl)- or -O-, and R^{30} and R^{31} are independently of each other, hydrogen, alkyl or heteroalkyl.

3. (Amended herein) The method of Claim 2 wherein R^1 and R^2 are hydrogen; and B is phenyl.

4. (Amended herein) The method of Claim 3 wherein A is phenyl.

5. (Amended herein) The method of Claim 4 wherein R^4 is hydrogen; and R^5 is halo or alkyl.

6. (Amended herein) The method of Claim 5 wherein R^5 is chloro, fluoro or methyl; and R^6 is hydrogen, chloro, fluoro, methyl or methoxy.

7. (Amended herein) The method of Claim 5, wherein R^3 is optionally substituted heteroaryl.

8. (Amended herein) The method of Claim 7, wherein R^3 is pyridin-2-yl, pyridin-3 yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted.

9. (Amended herein) The method of Claim 8, wherein R^3 is at the 3-position.

10. (Amended herein) The method of Claim 9, wherein R^5 is 4-F and R^6 is hydrogen.

11. (Amended herein) The method of Claim 9, wherein R^5 is 2-Me and R^6 is hydrogen.

12. (Amended herein) The method of Claim 5, wherein R^3 is optionally substituted phenyl.

13. (Amended herein) The method of Claim 12, wherein R^3 is 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl.

14. (Amended herein) The method of Claim 13, wherein R^3 is at the 3-position.

15. (Amended herein) The method of Claim 14, wherein R^5 is 4-F and R^6 is hydrogen.

16. (Amended herein) The method of Claim 5, wherein R^3 is:

(a) heteroalkyl;

(b) heteroalkoxy;

(c) heteroalkylamino;

(d) optionally substituted heterocyclylalkyl;

(e) optionally substituted heterocyclylalkoxy;

(f) optionally substituted heterocyclylalkylamino;

(g) -Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -$CONR^{12}R^{13}$, SO_2R^{14}, -$SO_2NR^{15}R^{16}$ -$NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl; or

(h) Z-alkylene-$NR^{30}R^{31}$ where Z is -NH-, -N(alkyl)- or -O-, and R^{30} and R^{31} are independently of each other, hydrogen, alkyl or heteroalkyl.

17. (Amended herein) The method of Claim 16, wherein R^3 is heteroalkyl.

18. (Amended herein) The method of Claim 17, wherein R^3 is at the 3-position and is selected from the group consisting of 2-dimethylaminoethyl, 3-dimethylaminopropyl, 4-dimethylaminobutyl, hydroxymethyl, 1,2-dihydroxyethyl, 3-hydroxy-3-methyl-1-butyl or 3-hydroxybutyl.

19. (Amended herein) The method of Claim 18, wherein R^5 is 2-F and R^6 is 4-F.

20. (Amended herein) The method of Claim 18, wherein R^5 is 4-F and R^6 is hydrogen.

21. (Amended herein) The method of Claim 18, wherein R^5 is 2-Me and R^6 is hydrogen.

22. (Amended herein) The method of Claim 16, wherein R^3 is heteroalkoxy or heteroalkylamino.

23. (Amended herein) The method of Claim 22, wherein R^3 is at the 3-position and is selected from the group consisting of 3-dimethylaminopropoxy, 2-dimethylaminoethoxy, 2-hydroxyethoxy, 2,3-dihydroxypropoxy, 2,2-(dihydroxymethyl)ethoxy, 2-dimethylaminoethylamino and 3-dimethylaminopropylamino.

24. (Amended herein) The method of Claim 23 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

25. (Amended herein) The method of Claim 16, wherein R^3 is optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkoxy or optionally substituted heterocyclylalkylamino.

26. (Amended herein) The method of Claim 25, wherein R^3 is at the 3-position and is selected from the group consisting of 3-(morpholin-4-yl)propoxy, 2-(morpholin-4-yl)ethoxy, 2-(2-oxo-pyrrolidin-1-yl)ethoxy, 3-(morpholin-4-yl)propyl, 2-(morpholin-4-yl)ethyl, 4-(morpholin-4-yl)butyl, 3-(morpholin-4-yl)propylamino, 2-(morpholin-4-yl)ethylamino, 4-hydroxy-piperidinylmethyl, 2-(S,S-dioxo-thiamorpholin-4-yl)ethyl, 3-(S,S-dioxo-thiamorpholin-4-yl)propyl and N-methylpiperazinylmethyl.

27. (Amended herein) The method of Claim 26 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

28. (Amended herein) The method of Claim 16 wherein R^3 is -Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -$CONR^{12}R^{13}$, SO_2R^{14}, -$SO_2NR^{15}R^{16}$ -$NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl.

29. (Amended herein) The method of Claim 28, wherein Y is a single bond and R^9 is SO_2R^{14} or -$SO_2NR^{15}R^{16}$.

30. (Amended herein) The method of Claim 29 wherein R^3 is methylsulfonylethyl or sulfamoylethyl.

31. (Amended herein) The method of Claim 30 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

REMARKS

This is a divisional application of the U.S. Application Serial No. No. 09/305,737, filed May 5, 1999, which claims the priority benefits of U.S. Provisional Application Serial No. 60/084,250, filed May 5, 1998, U.S. Provisional Application Serial No. 60/122,410, filed March 2, 1999, and U.S. Provisional Application Serial No. 60/130,369, filed April 21, 1999.

By the enclosed preliminary amendment, Claims 2-31 and 33 have been amended; and Claims 1, 32 and 36-37 have been canceled. Upon the entry of this Preliminary Amendment, Claims 2-31 and 33-35 will be pending in the present application.

Attached hereto is Appendix A captioned "Version with Markings to show changes made", and is a marked-up version of the changes made to the claims by the present amendment. In addition, for the convenience of the Examiner, all claims now pending following the entry of the present Preliminary Amendment are reproduced in Appendix B captioned "Pending Claims."

CONCLUSION

Applicants respectfully request that the application, as amended, be examined on its merits by the Examiner.

Respectfully submitted,

Mona Anand
Reg. No. 34,537
Attorney for Applicants

APPENDIX A
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

Please amend the text on page 1, lines 4-6 follows:

This application is a divisional application of U.S. Patent Application Serial No. 09/305,737, filed May 5, 1999 and claims the benefit under 35 U.S.C. 119(e) of U.S. Provisional Application Serial No. 60/084,250, filed May 5, 1998, U.S. Provisional Application Serial No. **[60/122,140]** 60/122,410, filed March 2, 1999, and U.S. Provisional Application Serial No. 60/130,369, filed April 21, 1999, all of which are incorporated herein by reference in their entirety.

IN THE CLAIMS

Claims 1, 32 and 36-37 have been canceled

2. (Amended) The ~~compound~~ method of Claim ~~1~~ 33 wherein R^3 is:

(a) optionally substituted heterocyclyl;

(b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO_2R' (where R' is alkyl) or $SO_2NHR'R''$ (where R' and R" are independently hydrogen or alkyl);

(c) heteroalkyl;

(d) heteroalkenyl;

(e) heteroalkylamino;

(f) heteroalkoxy;

(g) optionally substituted heterocyclylalkyl or heterocyclyloxy;

(h) optionally substituted heterocyclylalkenyl;

(i) optionally substituted heterocyclylalkynyl;

(j) optionally substituted heterocyclylalkoxy;

(k) optionally substituted heterocyclylalkylamino;

(l) optionally substituted heterocyclylalkylcarbonyl;

(k) -Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -$CONR^{12}R^{13}$, SO_2R^{14}, -$SO_2NR^{15}R^{16}$ -$NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl;

(l) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

(m) arylaminoalkylene or heteroarylaminoalkylene; or

(n) Z-alkylene-$NR^{30}R^{31}$ where Z is -NH-, -N(alkyl)- or -O-, and R^{30} and R^{31} are independently of each other, hydrogen, alkyl or heteroalkyl.

3. (Amended) The ~~compound~~ method of Claim 2 wherein R^1 and R^2 are hydrogen; and B is phenyl.

4. (Amended) The ~~compound~~ method of Claim 3 wherein A is phenyl.

5. (Amended) The ~~compound~~ method of Claim 4 wherein R^4 is hydrogen; and R^5 is halo or alkyl.

6. (Amended) The ~~compound~~ method of Claim 5 wherein R^5 is chloro, fluoro or methyl; and R^6 is hydrogen, chloro, fluoro, methyl or methoxy.

7. (Amended) The ~~compound~~ method of Claim 5, wherein R^3 is optionally substituted heteroaryl.

8. (Amended) The ~~compound~~ method of Claim 7, wherein R^3 is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted.

9. (Amended) The ~~compound~~ method of Claim 8, wherein R^3 is at the 3-position.

10. (Amended) The ~~compound~~ method of Claim 9, wherein R^5 is 4-F and R^6 is hydrogen.

11. (Amended) The ~~compound~~ method of Claim 9, wherein R^5 is 2-Me and R^6 is hydrogen.

12. (Amended) The ~~compound~~ method of Claim 5, wherein R^3 is optionally substituted phenyl.

13. (Amended) The ~~compound~~ method of Claim 12, wherein R^3 is 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl.

14. (Amended) The ~~compound~~ method of Claim 13, wherein R^3 is at the 3-position.

15. (Amended) The ~~compound~~ method of Claim 14, wherein R^5 is 4-F and R^6 is hydrogen.

16. (Amended) The ~~compound~~ method compound of Claim 5, wherein R^3 is:

(a) heteroalkyl;

(b) heteroalkoxy;

(c) heteroalkylamino;

(d) optionally substituted heterocyclylalkyl;

(e) optionally substituted heterocyclylalkoxy;

(f) optionally substituted heterocyclylalkylamino;

(f) -Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -$CONR^{12}R^{13}$, SO_2R^{14}, -$SO_2NR^{15}R^{16}$ -$NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl; or

(h) Z-alkylene-$NR^{30}R^{31}$ where Z is -NH-, -N(alkyl)- or -O-, and R^{30} and R^{31} are independently of each other, hydrogen, alkyl or heteroalkyl.

17. (Amended) The ~~compound~~ method of Claim 16, wherein R^3 is heteroalkyl.

18. (Amended) The ~~compound~~ method of Claim 17, wherein R^3 is at the 3-position and is selected from the group consisting of 2-dimethylaminoethyl, 3-dimethylaminopropyl, 4-dimethylaminobutyl, hydroxymethyl, 1,2-dihydroxyethyl, 3-hydroxy-3-methyl-1-butyl or 3-hydroxybutyl.

19. (Amended) The ~~compound~~ method of Claim 18, wherein R^5 is 2-F and R^6 is 4-F.

20. (Amended) The ~~compound~~ method of Claim 18, wherein R^5 is 4-F and R^6 is hydrogen.

21. (Amended) The ~~compound~~ method of Claim 18, wherein R^5 is 2-Me and R^6 is hydrogen.

22. (Amended) The ~~compound~~ method of Claim 16, wherein R^3 is heteroalkoxy or heteroalkylamino.

23. (Amended) The ~~compound~~ method of Claim 22, wherein R^3 is at the 3-position and is selected from the group consisting of 3-dimethylaminopropoxy, 2-dimethylaminoethoxy, 2-hydroxyethoxy, 2,3-dihydroxypropoxy, 2,2-(dihydroxymethyl)ethoxy, 2-dimethylaminoethylamino and 3-dimethylaminopropylamino.

24. (Amended) The ~~compound~~ method of Claim 23 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

25. (Amended) The ~~compound~~ method of Claim 16, wherein R^3 is optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkoxy or optionally substituted heterocyclylalkylamino.

26. (Amended) The ~~compound~~ method of Claim 25, wherein R^3 is at the 3-position and is selected from the group consisting of 3-(morpholin-4-yl)propoxy, 2-(morpholin-4-yl)ethoxy, 2-(2-oxo-pyrrolidin-1-yl)ethoxy, 3-(morpholin-4-yl)propyl, 2-(morpholin-4-yl)ethyl, 4-(morpholin-4-yl)butyl, 3-(morpholin-4-yl)propylamino, 2-(morpholin-4-yl)ethylamino, 4-hydorxy-piperidinylmethyl, 2-(S,S-dioxo-thiamorpholin-4-yl)ethyl, 3-(S,S-dioxo-thiamorpholin-4-yl)propyl and N-methylpiperazinylmethyl.

27. (Amended) The ~~compound~~ method of Claim 26 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

28. (Amended) The ~~compound~~ method compound of Claim16, wherein R^3 is at the 3-position and is selected from the group consisting of (2,2-dimethyl-1,3-dioxolan-4(S)-yl)methoxy, (1,3-dioxolan-2-on-4(R)-yl)methoxy, (2-thioxo-1,3-dioxolan-4-yl)methoxy, (2,2-diethyl-1,3-dioxolan-4(S)-yl)methoxy, (2,2-diethyl-1,3-dioxolan-4(S)-yl)methylamino and (2-methyl-2-ethyl-1,3-dioxolan-4(S)-yl)methoxy.

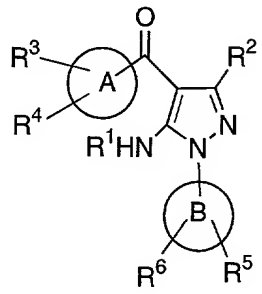
29. (Amended) The ~~compound~~ method of Claim 28 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

30. (Amended) The ~~compound~~ method of Claim 29, wherein Y is a single bond and R^9 is SO_2R^{14} or $-SO_2NR^{15}R^{16}$.

31. (Amended) The ~~compound~~ method of Claim 30 wherein R^3 is methylsulfonylethyl or sulfamoylethyl.

33. (Amended) A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a

therapeutically effective amount of a compound of ~~Claim 1.~~ selected from the group of compounds represented by Formula (I):



(I)

wherein:

R^1 is hydrogen or acyl;

R^2 is hydrogen or alkyl;

A is an aryl ring;

B is an aryl;

R^3 is selected from the group consisting of:

(a) amino, alkylamino or dialkylamino;

(b) acylamino;

(c) optionally substituted heterocyclyl;

(d) optionally substituted aryl or heteroaryl;

(e) heteroalkyl;

(f) heteroalkenyl;

(g) heteroalkynyl;

(h) heteroalkoxy;

(i) heteroalkylamino;

(j) optionally substituted heterocyclylalkyl;

(k) optionally substituted heterocyclylalkenyl;

(l) optionally substituted heterocyclylalkynyl;

(m) optionally substituted heterocyclylalkoxy, cycloalkoxy or heterocyclyloxy;

(n) optionally substituted heterocyclylalkylamino;

(o) optionally substituted heterocyclylalkylcarbonyl;

(p) heteroalkylcarbonyl;

(q) $-NHSO_2R^6$ where R^6 is alkyl, heteroalkyl or optionally substituted heterocyclylalkyl;

(r) $-NHSO_2NR^7R^8$ where R^7 and R^8 are, independently of each other, hydrogen, alkyl or heteroalkyl;

(s) -Y-(alkylene)-R^9 where:

Y is a single bond, -O-, -NH- or $-S(O)_n-$ (where n is an integer from 0 to 2); and

R^9 is cyano, optionally substituted heteroaryl, -COOH, $-COR^{10}$, $-COOR^{11}$, $-CONR^{12}R^{13}$, $-SO_2R^{14}$, $-SO_2NR^{15}R^{16}$, $-NHSO_2R^{17}$ or $-NHSO_2NR^{18}R^{19}$, where R^{10} is alkyl or optionally substituted heterocycle, R^{11} is alkyl, and R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18} and R^{19} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(t) $-C(=NR^{20})(NR^{21}R^{22})$ where R^{20}, R^{21} and R^{22} independently represent hydrogen, alkyl or hydroxy, or R^{20} and R^{21} together are $-(CH_2)_n-$ where n is 2 or 3 and R^{22} is hydrogen or alkyl;

(u) $-NHC(X)NR^{23}R^{24}$ where X is -O- or -S-, and R^{23} and R^{24} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(v) $-CONR^{25}R^{26}$ where R^{25} and R^{26} independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclylalkyl, or R^{25} and R^{26} together with the nitrogen to which they are attached form an optionally substituted heterocyclyl ring;

(w) $-S(O)_nR^{27}$ where n is an integer from 0 to 2, and R^{27} is alkyl, heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocyclylalkyl, or $-NR^{28}R^{29}$ where R^{28} and R^{29} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(x) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

(y) arylaminoalkylene or heteroarylaminoalkylene;

(z) Z-alkylene-$NR^{30}R^{31}$ or Z-alkylene-OR^{32} where Z is -NH-, -N(alkyl)- or -O-, and R^{30}, R^{31} and R^{32} are independently of each other, hydrogen, alkyl or heteroalkyl;

(aa) -OC(O)-alkylene-CO_2H or -OC(O)-NR'R" (where R' and R" are independently hydrogen or alkyl); and

(bb) heteroarylalkenylene or heteroarylalkynylene;

R^4 is selected from the group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl;

(d) alkoxy; and

(e) hydroxy;

R^5 is selected from the group consisting of :

(a) hydrogen;

(b) halo;

(c) alkyl;

(d) haloalkyl;

(e) thioalkyl;)

(f) hydroxy;

(g) amino;

(h) alkylamino;

(i) dialkylamino;

(j) heteroalkyl;

(k) optionally substituted heterocycle;

(l) optionally substituted heterocyclylalkyl;

(m) optionally substituted heterocyclylalkoxy;

(n) alkylsulfonyl;

(o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;

(p) heteroalkoxy; and

(q) carboxy;

R^6 is selected from a group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl; and

(d) alkoxy; and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

......*...*...*...*

APPENDIX B
PENDING CLAIMS

2. (Amended) The method of Claim 33 wherein R^3 is:

(a) optionally substituted heterocyclyl;

(b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO_2R' (where R' is alkyl) or $SO_2NHR'R''$ (where R' and R" are independently hydrogen or alkyl);

(c) heteroalkyl;

(d) heteroalkenyl;

(e) heteroalkylamino;

(f) heteroalkoxy;

(g) optionally substituted heterocyclylalkylor heterocyclyloxy;

(h) optionally substituted heterocyclylalkenyl;

(i) optionally substituted heterocyclylalkynyl;

(j) optionally substituted heterocyclylalkoxy;

(k) optionally substituted heterocylalkylamino;

(l) optionally substituted heterocyclylalkylcarbonyl;

(k) -Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -$CONR^{12}R^{13}$, SO_2R^{14}, -$SO_2NR^{15}R^{16}$ -$NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl;

(l) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

(m) arylaminoalkylene or heteroarylaminoalkylene; or

(n) Z-alkylene-$NR^{30}R^{31}$ where Z is -NH-, -N(alkyl)- or -O-, and R^{30} and R^{31} are independently of each other, hydrogen, alkyl or heteroalkyl.

3. (Amended) The method of Claim 2 wherein R^1 and R^2 are hydrogen; and B is phenyl.

4. (Amended) The method of Claim 3 wherein A is phenyl.

5. (Amended) The method of Claim 4 wherein R^4 is hydrogen; and R^5 is halo or alkyl.

6. (Amended) The method of Claim 5 wherein R^5 is chloro, fluoro or methyl; and R^6 is hydrogen, chloro, fluoro, methyl or methoxy.

7. (Amended) The method of Claim 5, wherein R^3 is optionally substituted heteroaryl.

8. (Amended) The method of Claim 7, wherein R^3 is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted.

9. (Amended) The method of Claim 8, wherein R^3 is at the 3-position.

10. (Amended) The method of Claim 9, wherein R^5 is 4-F and R^6 is hydrogen.

11. (Amended) The method of Claim 9, wherein R^5 is 2-Me and R^6 is hydrogen.

12. (Amended) The method of Claim 5, wherein R^3 is optionally substituted phenyl.

13. (Amended) The method of Claim 12, wherein R^3 is 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl.

14. (Amended) The method of Claim 13, wherein R^3 is at the 3-position.

15. (Amended) The methodd of Claim 14, wherein R^5 is 4-F and R^6 is hydrogen.

16. (Amended) The method of Claim 5, wherein R^3 is:

(a) heteroalkyl;

(b) heteroalkoxy;

(c) heteroalkylamino;

(d) optionally substituted heterocyclylalkyl;

(e) optionally substituted heterocyclylalkoxy; cycloalkoxy; or cycloalkylalkyloxy;

(f) optionally substituted heterocyclylalkylamino;

-Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -$CONR^{12}R^{13}$, SO_2R^{14}, -$SO_2NR^{15}R^{16}$ -$NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl; or

(h) Z-alkylene-$NR^{30}R^{31}$ where Z is -NH-, -N(alkyl)- or -O-, and R^{30} and R^{31} are independently of each other, hydrogen, alkyl or heteroalkyl.

17. (Amended) The method of Claim 16, wherein R^3 is heteroalkyl.

18. (Amended) The method of Claim 17, wherein R^3 is at the 3-position and is selected from the group consisting of 2-dimethylaminoethyl, 3-dimethylaminopropyl, 4-dimethylaminobutyl, hydroxymethyl, 1,2-dihydroxyethyl, 3-hydroxy-3-methyl-1-butyl or 3-hydroxybutyl.

19. (Amended) The method of Claim 18, wherein R^5 is 2-F and R^6 is 4-F.

20. (Amended) The method of Claim 18, wherein R^5 is 4-F and R^6 is hydrogen.

21. (Amended) The method of Claim 18, wherein R^5 is 2-Me and R^6 is hydrogen.

22. (Amended) The method of Claim 16, wherein R^3 is heteroalkoxy or heteroalkylamino.

23. (Amended) The method of Claim 22, wherein R^3 is at the 3-position and is selected from the group consisting of 3-dimethylaminopropoxy, 2-dimethylaminoethoxy, 2-hydroxyethoxy, 2,3-dihydroxypropoxy, 2,2-(dihydroxymethyl)ethoxy, 2-dimethylaminoethylamino and 3-dimethylaminopropylamino.

24. (Amended) The method of Claim 23 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

25. (Amended) The method of Claim 16, wherein R^3 is optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkoxy or optionally substituted heterocyclylalkylamino.

26. (Amended) The method of Claim 25, wherein R^3 is at the 3-position and is selected from the group consisting of 3-(morpholin-4-yl)propoxy, 2-(morpholin-4-yl)ethoxy, 2-(2-oxo-pyrrolidin-1-yl)ethoxy, 3-(morpholin-4-yl)propyl, 2-(morpholin-4-yl)ethyl, 4-(morpholin-4-yl)butyl, 3-(morpholin-4-yl)propylamino, 2-(morpholin-4-yl)ethylamino, 4-hydroxypiperidinylmethyl, 2-(S,S-dioxo-thiamorpholin-4-yl)ethyl, 3-(S,S-dioxo-thiamorpholin-4-yl)propyl and N-methylpiperazinylmethyl.

27. (Amended) The method of Claim 26 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

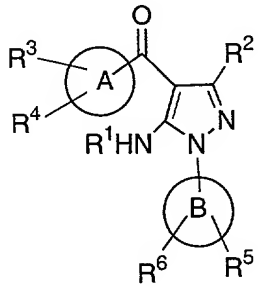
28. (Amended) The method of Claim 16 wherein R^3 is -Y-(alkylene)-R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -$CONR^{12}R^{13}$, SO_2R^{14}, -$SO_2NR^{15}R^{16}$ -$NHSO_2R^{17}$ or -$NHSO_2NR^{18}R^{19}$ where R^{12}, R^{13}, R^{14}, R^{15}, R^{16} R^{17}, R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl.

29. (Amended) The method of Claim 28, wherein Y is a single bond and R^9 is $-SO_2R^{14}$ or $-SO_2NR^{15}R^{16}$.

30. (Amended) The method of Claim 29 wherein R^3 is methylsulfonylethyl or sulfamoylethyl.

31. (Amended) The method of Claim 32 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

33. (Amended) A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound selected from the group of compounds represented by Formula (I):



(I)

wherein:

R^1 is hydrogen or acyl;

R^2 is hydrogen or alkyl;

A is an aryl ring;

B is an aryl ring;

R^3 is selected from the group consisting of:

(a) amino, alkylamino or dialkylamino;

(b) acylamino;

(c) optionally substituted heterocyclyl;

(d) optionally substituted aryl or heteroaryl;

(e) heteroalkyl;

(f) heteroalkenyl;

(g) heteroalkynyl;

(h) heteroalkoxy;

(i) heteroalkylamino;

(j) optionally substituted heterocyclylalkyl;

(k) optionally substituted heterocyclylalkenyl;

(l) optionally substituted heterocyclylalkynyl;

(m) optionally substituted heterocyclylalkoxy, cycloalkoxy, or heterocyclyloxy;

(n) optionally substituted heterocyclylalkylamino;

(o) optionally substituted heterocyclylalkylcarbonyl;

(p) heteroalkylcarbonyl;

(q) $-NHSO_2R^6$ where R^6 is alkyl, heteroalkyl or optionally substituted heterocyclylalkyl;

(r) $-NHSO_2NR^7R^8$ where R^7 and R^8 are, independently of each other, hydrogen, alkyl or heteroalkyl;

(s) -Y-(alkylene)-R^9 where:

Y is a single bond, -O-, -NH- or $-S(O)_n-$ (where n is an integer from 0 to 2); and

R^9 is cyano, optionally substituted heteroaryl, -COOH, $-COR^{10}$, $-COOR^{11}$, $-CONR^{12}R^{13}$, $-SO_2R^{14}$, $-SO_2NR^{15}R^{16}$, $-NHSO_2R^{17}$ or $-NHSO_2NR^{18}R^{19}$, where R^{10} is alkyl or optionally substituted heterocycle, R^{11} is alkyl, and R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18} and R^{19} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(t) $-C(=NR^{20})(NR^{21}R^{22})$ where R^{20}, R^{21} and R^{22} independently represent hydrogen, alkyl or hydroxy, or R^{20} and R^{21} together are $-(CH_2)_n-$ where n is 2 or 3 and R^{22} is hydrogen or alkyl;

(u) $-NHC(X)NR^{23}R^{24}$ where X is -O- or -S-, and R^{23} and R^{24} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(v) $-CONR^{25}R^{26}$ where R^{25} and R^{26} independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclylalkyl, or R^{25} and R^{26} together with the nitrogen to which they are attached form an optionally substituted heterocyclyl ring;

(w) $-S(O)_nR^{27}$ where n is an integer from 0 to 2, and R^{27} is alkyl, heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocyclylalkyl, or $-NR^{28}R^{29}$ where R^{28} and R^{29} are, independently of each other, hydrogen, alkyl or heteroalkyl;

(x) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

(y) arylaminoalkylene or heteroarylaminoalkylene;

(z) Z-alkylene-$NR^{30}R^{31}$ or Z-alkylene-OR^{32} where Z is -NH-, -N(alkyl)- or -O-, and R^{30}, R^{31} and R^{32} are independently of each other, hydrogen, alkyl or heteroalkyl;

(aa) $-OC(O)$-alkylene-CO_2H or -OC(O)-NR'R" (where R' and R" are independently hydrogen or alkyl); and

(bb) heteroarylalkenylene or heteroarylalkynylene;

R^4 is selected from the group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl;

(d) alkoxy; and

(e) hydroxy;

R^5 is selected from the group consisting of :

(a) hydrogen;

(b) halo;

(c) alkyl;

(d) haloalkyl;

(e) thioalkyl;

(f) hydroxy;

(g) amino;

(h) alkylamino;

(i) dialkylamino;

(j) heteroalkyl;

(k) optionally substituted heterocycle;

(l) optionally substituted heterocyclylalkyl;

(m) optionally substituted heterocyclylalkoxy;

(n) alkylsulfonyl;

(o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;

(p) heteroalkoxy; and

(q) carboxy;

R^6 is selected from a group consisting of:

(a) hydrogen;

(b) halo;

(c) alkyl; and

(d) alkoxy; and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

34. (As filed) The method of Claim 33 wherein the disease is an inflammatory disease.

35. (As filed) The method of Claim 34 wherein the disease is arthritis.

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